

pathological conditions are all perfectly well-known, but as was remarked in the introduction to this paper, we instinctively associate them with intracranial vascular disease.

It may add to our knowledge of encephalomalacia and the accuracy of vascular localization if the main vessel in the neck is also considered.

A STUDY OF THE VALUE OF THE QUANTITATIVE ESTIMATION OF DISSOLVED ALBUMIN IN GASTRIC EXTRACTS (WOLFF-JUNGHANS' TEST) IN THE DIAGNOSIS OF GASTRIC CANCER.

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METHODS for the estimation of the soluble albuminous products of digestion have frequently been devised with the hope that such might prove of practical service in the differential diagnosis of gastric ailments. Of these methods, the well-known procedure advanced by Solomon had for a time the greatest vogue. Esbach's reagent and tubes proved, however, unsatisfactory and inaccurate from a clinical view-point. More recently the problem has been approached from the practical quantitative side and encouraging work recorded.

Wolff and Junghans¹ report a method for estimation of the amount of soluble albumin in gastric extracts which they claim have given excellent clinical information in Ewald's service at the Augusta Hospital, Berlin.

Theoretically, their procedure has the following basis: In the normal aspirated test-meal there is demonstrable relatively large quantities of soluble albumin by means of precipitating reagents. This soluble albumin appears only through the agency of the gastric enzymes. This fact is proved by testing for soluble albumin a similar test-meal which has been chymified but not swallowed. In such event, only minute quantities of dissolved albumin are present.

Acting on these observed facts, Wolff and Junghans fed similar meals to sets of individuals revealing malignant and benign achylas. Their work appeared to show that in the malignant achylas, aspirated test meals were rich in soluble albumin, while in benign achylas very little of the albumin could be demonstrated.

¹ Berl. klin. Woch., May 29, 1911, and March 18, 1912; Medizinische Klinik, March 24, 1912; Taschenbuch der Magen und Darm Krankheiten, 1912.

Three suppositions have been advanced to explain this increased volume of dissolved albumin in the malignant achylia. It has been suggested that the excess of albumin is due (a) to interference with albuminous resorption; (b) to a "cancer milk" rich in albumin which exudes from malignant growths, and (c) to a specific, peptid-splitting ferment from the neoplasm, capable of carrying protein digestion as far as the completely soluble albumin stage.

Clinically, the reaction was shown to be positive in 18 of a series of 20 gastric cancers and negative in 14 of a series of 15 cases of simple achylia in Ewald's service. Recently, Rolph² has reported positive tests in all of 7 cases where cancer was present in the stomach or secondarily involved that viscus. In 8 cases of benign achylia the test proved negative. Rolph states that gastric contents contaminated with blood beyond a dilution of 1 to 3000 may give the reaction and cautions against positive interpretation in instances where there is high combined acid present. In such event peptone is usually present. He claims that cancer of the cardia is not so likely to give positive reaction as is cancer in other parts of the stomach.

AUTHOR'S STUDY. In the last 3950 patients presenting themselves for test-meal examination of gastric function in the Mayo Clinic, there were 747 instances where gastric extracts showed achylia or were associated with conditions likely to be confused with malignancy. These gastric extracts were all tested for soluble albumin by the Wolff-Junghans' method. Records were kept of the association of the results of this test with other test-meal and clinical findings. When the tabulations were completed the diagnoses were entered on the history sheets. In 78.4 per cent. of cases it was possible to obtain check upon diagnoses by operation.

Selection of Material and Mode of Procedure. The day previous to the examination of his gastric extract the patient was given 1 ounce of castor oil at 4 P.M. This was followed at 6 P.M. by a motor test-meal consisting of mixed food. At 7 P.M. twenty raw, seedless raisins were given. Twelve hours later (7 A.M. the following morning) the patient was fed 60 grams of second-day bread and 200 c.c. of water. This secretory test-meal was removed from fifty to sixty minutes after administering. The specimen secured was thoroughly mixed, filtered through double hydrochloric-acid-washed papers, and tested for dissolved albumin within an hour of its being obtained from the stomach. On account of the fact that, as has been shown in this clinic,³ but 52.2 per cent. of cases of gastric cancer yield gastric extracts revealing absence of free hydrochloric acid, and that in 15.7 per cent. of cases, free hydro-

² Med. Record, New York, May 10, 1913, p. 849.

³ Smithies, The Significance of Gastric Ulcer with Respect to Gastric Cancer, Jour. Amer. Med. Assoc., November 15, 1913, p. 1793.

chloric acid ranges between 20 and 50 per cent., we have deemed it advisable to apply the test for soluble albumin not only to achylas, but also to gastric extracts where the free hydrochloric acid was below 20 per cent. In a few instances of suspected malignant ulcer we have performed the test upon gastric extracts with higher free hydrochloric acid content. In such we have been fully alive to the possibilities of error, but for the purpose of gaining information and for comparison we have deemed it wise to make the test.

Procedure. Six absolutely clean test-tubes are required for each test. Those of the narrow type and of 20 c.c. capacity answer very well. The tubes are numbered serially from 1 to 6. They receive respectively 1 c.c., 0.5 c.c., 0.25 c.c., 0.1 c.c., 0.05 c.c. and 0.025 c.c. of the filtered gastric extract. These amounts are readily measured by means of a 1 c.c. pipette, graduated in $1-\frac{1}{100}$ c.c. By means of a 10 c.c. pipette, graduated into $1-\frac{1}{10}$ c.c., the volume in each test-tube is next consecutively brought up to 10 c.c. volume with distilled water. This gives from the tubes 1 to 6 dilutions of gastric juice varying respectively from 1 to 10 to 1 to 400 (viz., 1 to 10, 1 to 20, 1 to 40, 1 to 100, 1 to 200, and 1 to 400). These figures we have termed "units" of precipitable albumin. The tubes are then inverted several times to insure complete mixture of their contents. One c.c. of the reagent to precipitate the albumin in solution is then carefully layered upon the contents of each tube. The precipitating reagent suggested by Wolff has proved satisfactory with us. It has the following formula:

Phosphotungstic acid (puriss).	3 c.c.
Hydrochloric acid (concentrated)	10 c.c.
Alcohol (96 per cent.)	200 c.c.
Aq. dest.	q. s. ad 2000 c.c.

Mix and keep in a glass or rubber-stoppered flask in a cool place.

Manifestation and Interpretation of the Test. If there has been dissolved albumin in any of the tubes, the juncture of the Wolff reagent with the diluted gastric extracts is marked by a pearly white zone or "ring." This is better brought out if the tubes are inspected against a black background. (We have used a piece of black cloth such as photographers employ when focussing cameras.) The tubes should be inspected at once after adding the Wolff solution. Prolonged standing allows cloudy zones to form which render comparative interpretation dubious.

We have interpreted our results after Wolff and Junghans' suggestion. If the white ring of precipitated albumin appears in tubes 1, 2, and 3 (namely, units of albumin from 10 up to 50) and no further manifestations are present in the remaining three tubes we have called the test negative. If tubes 1, 2, 3, and 4 exhibit rings (units of albumin from 10 to 100) we have considered the

reaction doubtful. The presence of white rings in tubes 1, 2, 3, 4, 5 and above (units of albumin ranging from 10 to 200 to 400) we have taken to denote a positive test.

Results. The gross results of our work are as follows: Of 747 gastric extracts of the class described above, 318 (42.6 per cent.) gave 200 to 400 units of precipitable albumin; 112 (15.7 per cent.) exhibited 100 units, and 317 (42.4 per cent.) showed less than 100 units. In this grouping, 71.5 per cent. of the gastric extracts were from cases showing some degree of gastric retention.

Consideration of Cancer Cases. There were 215 cases of operatively and pathologically demonstrated gastric carcinoma in this series. In 141 (65.1 per cent.) units of precipitable albumin ranged from 200 to 400. In 29 instances (13.4 per cent.) there were 100 units of albumin shown. Combining the returns it is evident that 170 (78.5 per cent.) of the proved cases of gastric cancer gave either undoubtedly positive or suspiciously positive Wolff-Junghans' test. In 45 cases (21 per cent.) the test was negative, less than 100 units of precipitable albumin being demonstrated. Of this group of 215 cases of gastric cancer, 73.2 per cent. exhibited some grade of motor stagnation.

Gastric extracts from 15 cases of *ulcus carcinomatosum* were tested. In 11 instances (73.3 per cent.) units of precipitable albumin ranged between 200 to 400. In 3 (20 per cent.), 100 units were shown. In other words, of the 15 cases of malignant gastric ulcer, 14 (93.3 per cent.) were either definitely positive or suspiciously so to the Wolff-Junghans' test. One case (6.6 per cent.) exhibited below 100 units of albumin. In this group, motor stagnation of some degree was present in 86.6 per cent.

Combining the results from the cases of frank gastric carcinoma and those of *ulcus carcinomatosum*, it is seen that of a total of 230 cases, 184 (80 per cent.) returned positive or suspicious Wolff-Junghans' test.

Relation of Manifestations of Test to Location of Malignant Process. We examined gastric extracts from 10 cases of cancer involving the cardia. Six cases (60 per cent.) gave positive test, 1 (10 per cent.) was suspicious, and 3 (30 per cent.) were negative. Thus 70 per cent. of our cases of cancer at the cardia showed units of precipitable albumin ranging from 100 to 400.

There were 5 cases of cancer of the fundus in our series; 1 (20 per cent.) was positive, 1 (20 per cent.) was doubtful, and 3 (60 per cent.) were negative.

We have records of 44 cases where the neoplasm involved mainly the lesser curvature of the stomach. Of this group, 33 cases (75 per cent.) gave clearly positive Wolff-Junghans' test, 4 (9.1 per cent.) were suspicious, and 7 (15.8 per cent.) were negative. It is evident that 84.1 per cent. of cancers involving the lesser curvature show units of precipitable albumin ranging from 100 upward.

In our series there were 3 cases of cancer of the greater curvature. Two cases (66.6 per cent.) were positive and the remaining case suspicious. Thus all showed 100 plus units of albumin.

Eight of our cases were proved to have cancer involving mainly the posterior wall of the stomach. Of this group but 3 cases (37.5 per cent.) were positive to the test, while 5 cases (62.5 per cent.) were negative.

The pars media was involved 14 times. Of this number, 11 cases (78.5 per cent.) gave positive test and 3 cases (21.5 per cent.) were negative.

In 93 instances the malignant growth was at the pylorus and antrum. In this class, 59 cases (63.4 per cent.) showed units of precipitable albumin from 200 upward, 8 cases (8.6 per cent.) were suspicious, revealing 100 units, and 25 cases (26.9 per cent.) were negative. In other words, 72 per cent. of the cancers at the pyloric region gave a positive or suspicious Wolff-Junghans' test.

Our series includes 38 cases where the stomach showed general or extensive malignant involvement. In 26 instances (68.5 per cent.) the test was positive, in 3 cases (7.9 per cent.) it was suspicious, while 9 times (23.6 per cent.) negative results were obtained.

Comparison of Other Test-meal Findings in the Cancer Cases with the Wolff-Junghans' Test. It might be profitable here to emphasize the diagnostic relation of other tests associated with that for dissolved albumin in the gastric extracts from our malignant cases. It will be noted above that of the 230 cancer and malignant ulcer cases the Wolff-Junghans' test was positive or suspicious in 184 (80 per cent.). In this same group of cases, free hydrochloric acid was absent in 52.2 per cent., lactic acid was demonstrated in 48.8 per cent., "occult" or altered blood shown in 75 per cent., glycyltryptophan test present in 40 per cent. (141 cases), the average formal index (method of Sorenson and Schiff⁴) was 21 (57 cases), and organisms of the Boas-Oppler group were demonstrated in 93.8 per cent. (146 cases) by the colored agar method.⁵ Some degree of gastric retention was shown in nearly 74 per cent. of the entire group of cancer cases, irrespective of the location of the growth.

The Wolff-Junghans' Test in Extragastric Cancer: Liver and Gall Tract. Our series includes 15 instances of malignancy in this location. In 5 cases (33.3 per cent.) the test was positive, in 3 cases (20 per cent.) it was suspicious, and in 7 cases (46.6 per cent.) it was negative. Thus 8 cases (53.3 per cent.) of extragastric malignancy showed units of albumin from 100 upward. Some degree of motor stagnation was evidenced in 26.6 per cent. of these cases.

The *pancreas* was the seat of malignant processes three times.

⁴ Zeitschrift für physiologische Chemie, 1909, xiii, 27.

⁵ Smithies, Arch. Int. Med., June, 1911, p. 736.

In no instance was a positive Wolff-Junghans' test obtained. Motor defect was not noted in any of these cases.

There was 1 case of cancer of the *transverse colon*. It gave a negative test. There was normal gastric motility in this case.

Gastric Syphilis. We have tested gastric extracts for dissolved albumin from 5 cases. The reaction was positive in 2 instances (40 per cent.), suspicious in 1 (20 per cent.), and negative in 2 (40 per cent.). In one of the positive cases the specific process in the stomach was associated with multiple and exuberant ulceration. Gastric motility was interfered with in 1 case (20 per cent.) of this group.

Primary Anemias (mainly pernicious). Twenty-four cases of achylia in severe anemia comprised this class. In none of them was gastric stagnation present. Twenty-three (95.6 per cent.) of this group were negative to the Wolff-Junghans' test. In but 1 instance (3.3 per cent.) were the units of precipitable albumin above 200.

Simple Achylia Gastrica. We examined gastric extracts from 35 such cases. Gastric stagnation was proved in 4 cases (11.9 per cent.). In 22 instances (63 per cent.) of this type of achylia the test was negative, in 9 instances (25.9 per cent.) suspicious, and positive but 4 times (11.9 per cent.).

Achylorhydria. In addition to the cases of absent free hydrochloric acid mentioned in the above groups there were 212 cases of non-malignant disease showing achylorhydria. Gastric motility was impaired in 22 cases (10.3 per cent.). In this group 136 cases (64.1 per cent.) were Wolff-Junghans negative, 41 cases (19.3 per cent.) were doubtful, and 35 cases (16.5 per cent.) were positive.

Simple Gastric Ulcer. A number of cases of this affection and of duodenal ulcer were studied for purposes of comparison with the malignant cases. Their gastric extracts generally showed low free hydrochloric acid content. We tested extracts from 33 cases of operatively demonstrated gastric ulcer for dissolved albumin. In 16 instances (48.4 per cent.) units of albumin ranged above 200, in 6 instances (18.1 per cent.) the units ran as high as 100, while in 11 cases (30.3 per cent.) units of albumin were below 100. It is thus apparent that 66.5 per cent. of the proved cases of simple gastric ulcer were positive or suspicious to the Wolff-Junghans' test. Gastric motility was delayed in 39.4 per cent. of this group.

Duodenal Ulcer. Gastric extracts from 18 cases of duodenal ulcer were tested. In 12 cases (66.6 per cent.) units of albumin ranged above 200, in 2 cases (11 per cent.) at least 100 units were present, while 4 times (22.7 per cent.) less than 100 units were demonstrated. It is thus evident that 78 per cent. of our cases of duodenal ulcer were Wolff-Junghans' positive or suspicious. In this group, gastric stagnation was present in 55.5 per cent. of the cases.

Nephritis and Cardiovascular Disease. Our series include 12 cases of cardiorenal affections associated with obscure gastric complaint and anemia. The gastric extracts showed achylia. In 6 instances (50 per cent.) the Wolff-Junghans' test was doubtful, while in an equal number it was negative. The doubtful cases were associated with some degree of gastric motor insufficiency.

Cases Exhibiting Low Gastric Acidity. In this group we include 159 instances where gastric acidity ranged from 2 to 70. The average was 18.7. This group furnished what might be regarded as controls on our reactions in other groups, as well as demonstrated what results might be expected from the Wolff-Junghans' test in extragastric, malignant, and non-malignant ailments. It should be emphasized that all of the patients examined complained of some gastric disturbance. The finding of the low free hydrochloric acid in some instances might have led to suspicions of malignancy by those who hold gastric acidity as a strong index of such condition. This might have been especially so when we recall that the average age of our patients is above forty years.

Clinically, this group was varied as to diagnosis. Among the affections were appendicitis, cholecystitis, cholelithiasis, alcoholic gastritis, gastric neuroses, pulmonary tuberculosis, tabes, multiple sclerosis, tuberculous peritonitis, nephrolithiasis, pancreatitis, cirrhosis of the liver, pregnancy, malaria, diabetes, aneurysm of the abdominal aorta, chronic constipation, hemophilia, cancer of the breast, cancer of the lip, etc.

Of this heterogeneous group of low gastric acidity cases, 40 (25.1 per cent.) were Wolff-Junghans' positive, 38 (23.9 per cent.) were doubtful, and 81 (50.9 per cent.) were negative. In other words, of this class nearly 50 per cent. of cases showed units of precipitable albumin from 100 upward. Gastric motility was interfered with in some degree in 25 cases (15.7 per cent.).

Relation of the Wolff-Junghans' Test to the Presence of Blood in Gastric Extracts. We have frequently tested gastric contents that were discolored bright red by traumatic blood without getting positive Wolff-Junghans' tests. Of our entire series of 747 cases herewith detailed, "occult" blood was demonstrated by the benzidin test in 43.2 per cent. Reference to the gross summary of our work above will reveal the fact that we obtained positive tests for precipitable albumin in 42.6 per cent. of the gastric extracts of the entire series, while in 15 per cent. the test was doubtful. There may be more than a curious relationship between these groups of figures.

SUMMARY. The work herewith submitted appears to justify the following conclusions:

1. When carefully performed and interpreted the Wolff-Junghans' test for demonstration of dissolved albumin in gastric extracts was positive or suspicious in 80 per cent. of our series of gastric

cancer. In this series it was a more constant finding in gastric extracts than were absent free hydrochloric acid, the presence of lactic acid, and the glycytryptophan test. It was rather more constant than tests for occult blood and the demonstration of gastric motor inefficiency. It was not so consistent in its manifestation as the demonstration of organisms of the Boas-Oppler group or the increase in the formol index.

2. In extragastric malignancy, gastric syphilis, and nephritis the Wolff-Junghans' test is inconstant.

3. In the differentiation between malignant and non-malignant achylia the Wolff-Junghans' test, when interpreted in connection with other clinical and laboratory data, is of considerable value. Positive reactions are rarely obtained in the achylia of primary anemia, simple achylia gastrica, and simple achlorhydria when such are unassociated with gastric motor inefficiency.

4. Simple gastric and duodenal ulcers, especially when accompanied by pyloric stenosis or gastric atony, may give confusing responses to the Wolff-Junghans' test.

5. The presence of blood in gastric extracts may be a factor in the production of certain atypical positive tests.

JAUNDICE IN TUBERCULOSIS.

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JAUNDICE is caused by the presence of bile pigment in the blood. It is now acknowledged that the passage of the bile pigment is by way of the lymphatics into the thoracic duct and thus into the general circulation, and is always caused by some obstruction, whether extrahepatic or intrahepatic, to the normal flow of the bile. Rolleston divides jaundice into: "(1) Extrahepatic or 'obstructive' where there is a gross obstruction, usually involving the larger extrahepatic bile ducts, to the flow of bile along the bile ducts. (2) Toxemic, intrahepatic, or hemohepatogenous, where there is obstruction in the small intrahepatic bile ducts. The obstruction is due to cholangitis or inflammation of the minute ducts, depending upon the irritating effect of poisons derived from the blood circulating through the liver." In tuberculosis we find jaundice caused by both extrahepatic and intrahepatic obstruction to the flow of bile.